PADUA DAYS ON MUSCLE AND MOBILITY MEDICINE 2026

International Conference

March 3rd to 6th Euganean Thermae and Padua, Italy

LECTURE: SEX HORMONES AND SKELETAL MUSCLE FUNCTION WITH AGING AND CANCER: THE GONAD-BONE-MUSCLE AXIS

James Carson

Integrative Muscle Biology Lab, Huffines Institute for Sports Medicine & Human Performance, Texas A&M University, College Station, Texas, USA.

Our adult population's metabolic health and overall functional capacity are directly linked to skeletal muscle mass maintenance (1-4). Furthermore, skeletal muscle loss and metabolic dysfunction that can occur in many disease conditions can impact patient survival, health, and quality of life, key outcomes for successful treatment (2,3). We know that muscle mass and metabolic properties are related to a variety of factors, including muscle loading and activity levels, nutrition, and hormones (5). Consequently, maintaining muscle mass and regrowing it after atrophy have become a critical goal for many adults due to periods of forced immobility, sedentary behavior, and chronic disease. There is a need for new strategies and approaches to improve muscle accretion in individuals with low muscle mass, as well as for novel therapeutic targets to enhance muscle mass recovery from atrophy (6). The emerging view of muscle mass regulation across many conditions involves the integration of multiple stimuli, synthesized by intracellular pathways and processes, into a muscle anabolic or catabolic response that results in muscle accretion or loss (7). Furthermore, healthy skeletal muscle is highly responsive to systemic and microenvironmental factors. Hormonal and growth factor stimuli, including testosterone, IGF-1, and Growth Hormone, have established roles in regulating muscle growth. While less acknowledged, estrogen is also a potent regulator of muscle mass and metabolism (4,8). Interestingly, while hypogonadism is a hallmark of many conditions and diseases that induce muscle wasting (1,4), it has received much less attention from the scientific community compared to factors such as chronic inflammation or insulin resistance. An improved understanding of the contribution of hypogonadism in males and females to muscle wasting in many conditions has critical clinical implications for human health. While there has been significant advancement in understanding the molecular drivers of hormone-induced muscle hypertrophy, the repercussions for muscle mass loss and recovery in many conditions are multifactorial and more challenging to target. The regulation of muscle mass by hormones and growth factors remains an active area of inquiry. The muscle environment can also involve crosstalk between tissues, such as bone, and target many muscle cell types, including myofibers, satellite cells, immune cells, endothelial cells, and fibroblasts. The presentation will highlight the importance of gonadal function for maintaining muscle mass in conditions such as cancer. Specific examples will be provided for the critical role of the ovary in skeletal muscle regulation of mass and metabolism in the female, which can be disrupted by several factors, including cancer and treatment.

Keywords: *sarcopenia, muscle wasting, hypogonadism, estrogen, cachexia.*

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